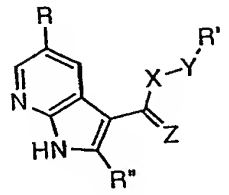
Claims

1. A compound of formula (I) as defined below:



(I)

wherein:

R stands for carbocyclyl, substituted carbocyclyl, heterocyclyl, or substituted heterocyclyl, wherein

the optionally substituted carbocyclyl or optionally substituted heterocyclyl group is optionally fused to an unsaturated, partially unsaturated or fully saturated five to seven membered ring containing zero to three heteroatoms,

each substitutable carbon atom in R, including the optional fused ring, is optionally and independently substituted by one or more of $C_{1\text{-}12}$ alkyl, carbocyclyl, or heterocyclyl, halogen, haloalkyl, OR^2, SR^2, NO_2, CN, NR^2R^2, NR^2COR^2, $NR^2CONR^2R^2$, NR^2COR^2, $NR^2CO_2R^2$, CO_2R^2, COR^2, $CONR^2R^2$, $S(O)_2R^2$, $SONH_2$, $S(O)R^2$, $SO_2NR^2R^2$, $NR^2S(O)_2R^2$, wherein each R^2 may be the same or different and is as defined below and wherein:

the $C_{1\text{-}12}$ alkyl optionally incorporates one or two insertions selected from the group consisting of -O-, -C(O)-, -N(R^2)-, -S(O)- and –$S(O_2)$- wherein each R^2 may be the same or different and is as defined below;

the $C_{1\text{-}12}$ alkyl, carbocyclyl, or heterocyclyl group is optionally substituted by one or more of halogen, haloalkyl, OR^2, SR^2, NO_2, CN, NR^2R^2, NR^2COR^2, $NR^2CONR^2R^2$, NR^2COR^2, $NR^2CO_2R^2$, CO_2R^2, COR^2, $CONR^2R^2$, $S(O)_2R^2$, $SONH_2$, $S(O)R^2$, $SO_2NR^2R^2$, $NR^2S(O)_2R^2$; wherein each R^2 may be the same or different and is as defined below and

the carbocyclyl, or heterocyclyl group is optionally substituted by one or more C_{1-12} alkyl,

each saturated carbon in the optional fused ring is further optionally and independently substituted by =O, =S, $=NNHR^2$, NNR^2R^2, $=N\text{-}OR^2$, $=NNHCOR^2$, $=NNHCO_2R^2$, $=NNSO_2R^2$, or $=NR^2$, wherein each R^2 may be the same or different and is as defined below; and

each substitutable nitrogen atom in R is optionally substituted by R^3, COR^2, SO_2R^2 or CO_2R^2, wherein each R^2 and R^3 may be the same or different and is as defined below;

R^2 is hydrogen , C_{1-12} alkyl or aryl, optionally substituted by one or more of C_{1-4} alkyl, halogen, C_{1-4} haloalkyl, OR^4, SR^4, NO_2, CN, NR^4R^4, NR^4COR^4, $NR^4CONR^4R^4$, NR^4COR^4, $NR^4CO_2R^4$, CO_2R^4, COR^4, $CONR^4{}_2$, $S(O)_2R^4$, $SONH_2$, $S(O)R^4$, SO_2 NR^4R^4, $NR^4S(O)_2R^4$, wherein the C_{1-12} alkyl group optionally incorporates one or two insertions selected from the group consisting of -O-, $-N(R^4)-$, -S(O)- and $-S(O_2)-$, wherein each R^4 may be the same or different and is as defined below;

R^3 is C_{1-12} alkyl or aryl, optionally substituted by one or more of C_{1-4} alkyl, halogen, C_{1-4} haloalkyl, OR^4, SR^4, NO_2, CN, NR^4R^4, NR^4COR^4, $NR^4CONR^4R^4$, NR^4COR^4, $NR^4CO_2R^4$, CO_2R^4, COR^4, $CONR^4{}_2$, $S(O)_2R^4$, $SONH_2$, $S(O)R^4$, SO_2 NR^4R^4, $NR^4S(O)_2R^4$, wherein the C_{1-12} alkyl group optionally incorporates one or two insertions selected from the group consisting of -O-, $-N(R^4)-$, -S(O)- and $-S(O_2)-$, wherein each R^4 may be the same or different and is as defined below;

R^4 is hydrogen, C_{1-4} alkyl, or C_{1-4} haloalkyl;

R' is C_{1-12} alkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, carbocyclyl or heterocyclyl, each of which is optionally substituted, wherein:

the optionally substituted carbocyclyl or heterocyclyl group is optionally fused to one to three unsaturated, partially unsaturated or fully saturated five to seven membered rings containing zero to three heteroatoms,

each substitutable carbon atom in R', including the optional fused ring, is optionally and independently substituted by one or more

of C_{1-12} alkyl, C_{3-12} cycloalkyl, C_{3-12} heterocycloalkyl, aryl, heteroaryl halogen, haloalkyl, OR^2, SR^2, NO_2, CN, NR^2R^2, NR^2COR^2, $NR^2CONR^2R^2$, NR^2COR^2, $NR^2CO_2R^2$, CO_2R^2, COR^2, $CONR^2R^2$, $S(O)_2R^2$, $SONH_2$, $S(O)R^2$, SO_2 NR^2R^2, $NR^2S(O)_2R^2$, wherein each R^2 may be the same or different and is as defined above and wherein:

the C_{1-12} alkyl group optionally incorporates one or two insertions selected from the group consisting of -O-, -C(O)-, -$N(R^2)$-, -S(O)- and –$S(O_2)$-, wherein each R^2 may be the same or different and is as defined above;

the C_{1-12} alkyl, C_{3-12} cycloalkyl, C_{3-12} heterocycloalkyl, aryl, or heteroaryl groups are optionally substituted by one or more of halogen, haloalkyl, OR^2, SR^2, NO_2, CN, NR^2R^2, NR^2COR^2, $NR^2CONR^2R^2$, NR^2COR^2, $NR^2CO_2R^2$, CO_2R^2, COR^2, $CONR^2R^2$, $S(O)_2R^2$, $SONH_2$, $S(O)R^2$, $SO_2NR^2R^2$, $NR^2S(O)_2R^2$, wherein each R^2 may be the same or different and is as defined above; and

the C_{3-12} cycloalkyl, C_{3-12} heterocycloalkyl, aryl, or heteroaryl groups are optionally substituted by one or more C_{1-12} alkyl groups;

each saturated carbon in R', including the optional fused ring, is further optionally and independently substituted by =O, =S, NNR^2R^2, =N-OR^2, =$NNHCOR^2$, =$NNHCO_2R^2$, =$NNSO_2R^2$, or =NR^2, wherein each R^2 may be the same or different and is as defined above; and

each substitutable nitrogen atom in R' is optionally substituted by R^3, COR^2, SO_2R^2 or CO_2R^2 wherein each R^2 and R^3 may be the same or different and is as defined above;

R" is hydrogen, C_{1-12} alkyl, carbocyclyl or heterocyclyl, each of which is optionally substituted, wherein:

the said carbocyclyl or heterocyclyl is optionally fused to one to three unsaturated, partially unsaturated or fully saturated five to seven membered ring containing zero to three heteroatoms,

each substitutable carbon atom in R'', including the optional fused ring, is optionally and independently substituted by one or more of C_{1-12} alkyl, C_{3-12} cycloalkyl, C_{3-12} heterocycloalkyl, aryl, heteroaryl, halogen, haloalkyl, OR^2, SR^2, NO_2, CN, NR^2R^2, NR^2COR^2, $NR^2CONR^2R^2$, NR^2COR^2, $NR^2CO_2R^2$, CO_2R^2, COR^2, $CONR^2R^2$, $S(O)_2R^2$, $SONH_2$, $S(O)R^2$, SO_2 NR^2R^2, $NR^2S(O)_2R^2$, wherein each R^2 may be the same or different and is as defined below and wherein:

the C_{1-12} alkyl group optionally incorporate one or two insertions selected from the group consisting of -O-, -C(O)-, -N(R^2)-, -S(O)- and –S(O_2)-;

the C_{1-12} alkyl, C_{3-12} cycloalkyl, C_{3-12} heterocycloalkyl, aryl, and heteroaryl groups are optionally substituted by one or more of halogen, haloalkyl, unsaturated or partly saturated cycloalkyl, aryl, or heteroaryl, OR^2, SR^2, NO_2, CN, NR^2R^2, NR^2COR^2, $NR^2CONR^2R^2$, NR^2COR^2, $NR^2CO_2R^2$, CO_2R^2, COR^2, $CONR^2R^2$, $S(O)_2R^2$, $SONH_2$, $S(O)R^2$, SO_2 NR^2R^2, $NR^2S(O)_2R^2$, wherein each R^2 may be the same or different and is as defined above; and

the C_{3-12} cycloalkyl, C_{3-12} heterocycloalkyl, aryl, and heteroaryl groups, are optionally substituted by one or more C_{1-12} alkyl

each saturated carbon in R'', including the optional fused ring, is further optionally and independently substituted by =O, =S, NNR^2R^2, =N-OR^2, =NNHCOR^2, =NNHCO_2R^2, =NNSO_2R^2, or =NR^2, wherein each R^2 may be the same or different and is as defined above; and

each substitutable nitrogen atom in R'' is optionally substituted by R^3, COR^2, SO_2 R^2 or CO_2 R^2, wherein each R^2 and R^3 may be the same or different and is as defined above;

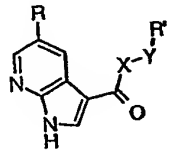
X is NR^5; O, S or C_{1-4} alkylene that is optionally substituted by one or more of halogen, haloalkyl, OR^2, SR^2, NO_2, CN, NR^2R^2, NR^2COR^2, $NR^2CONR^2R^2$, NR^2COR^2, $NR^2CO_2R^2$, CO_2R^2, COR^2, $CONR^2R^2$, $S(O)_2R^2$, $SONH_2$, $S(O)R^2$, $SO_2NR^2R^2$, $NR^2S(O)_2R^2$, wherein each R^2 may be the same or different and is as defined above and R^5 is H, C_{1-4} alkyl, C_{1-4} alkoxy, C_{1-4} haloalkyl or C_{1-4} haloalkyl; and

Y is absent or is NR^6, O, CR^6R^6, or C_{1-4} alkylene wherein each R^6 may be the same or different and is H, C_{1-4} alkyl, C_{1-4} alkoxy or C_{1-4} haloalkyl; and

Z is O, S or NR^7 wherein each R^7 may be the same or different and is hydrogen, C_{1-4} alkyl optionally substituted with one or more of halide, OR^8, NR^8R^8 or aryl, where each R^8 may be the same or different and stand for H, C_{1-4} alkyl, C_{1-4} alkoxy, C_{1-4} haloalkyl or C_{1-4} haloalkoxy;

and the pharmaceutically acceptable salts, and other pharmaceutically acceptable biohydrolyzable derivatives thereof, including esters, amides, carbamates, carbonates, ureides, solvates, hydrates, affinity reagents or prodrugs thereof.

2. A compound as claimed in claim 1, having the formula (Ia);



(Ia)

wherein

R stands for carbocyclyl, substituted carbocyclyl, heterocyclyl, or substituted heterocyclyl, wherein

the optionally substituted carbocyclyl or optionally substituted heterocyclyl group is optionally fused to an unsaturated, partially unsaturated or fully saturated five to seven membered ring containing zero to three heteroatoms,

each substitutable carbon atom in R, including the optional fused ring, is optionally and independently substituted by one or more of C_{1-12} alkyl, carbocyclyl, or heterocyclyl, halogen, haloalkyl, OR^2, SR^2, NO_2, CN, NR^2R^2, NR^2COR^2, $NR^2CONR^2R^2$, NR^2COR^2, $NR^2CO_2R^2$, CO_2R^2, COR^2, $CONR^2R^2$, $S(O)_2R^2$, $SONH_2$, $S(O)R^2$, $SO_2NR^2R^2$, $NR^2S(O)_2R^2$, wherein each R^2 may be the same or different and is as defined below and wherein:

the C_{1-12} alkyl optionally incorporates one or two insertions selected from the group consisting of -O-, -C(O)-, -N(R^2)-, -S(O)- and –S(O_2)- wherein each R^2 may be the same or different and is as defined below;

the C_{1-12} alkyl, carbocyclyl, or heterocyclyl group is optionally substituted by one or more of halogen, haloalkyl, OR^2, SR^2, NO_2, CN, NR^2R^2, NR^2COR^2, $NR^2CONR^2R^2$, NR^2COR^2, $NR^2CO_2R^2$, CO_2R^2, COR^2, $CONR^2R^2$, $S(O)_2R^2$, $SONH_2$, $S(O)R^2$, $SO_2NR^2R^2$, $NR^2S(O)_2R^2$; wherein each R^2 may be the same or different and is as defined below and

the carbocyclyl, or heterocyclyl group is optionally substituted by one or more C_{1-12} alkyl,

each saturated carbon in the optional fused ring is further optionally and independently substituted by =O, =S, =NNHR^2, NNR^{2}R^2, =N-OR^2, =NNHCOR^2, =NNHCO$_2$R^2, =NNSO$_2$R^2, or =NR^2, wherein each R^2 may be the same or different and is as defined below; and

each substitutable nitrogen atom in R is optionally substituted by R^3, COR^2, SO_2R^2 or CO_2R^2, wherein each R^2 and R^3 may be the same or different and is as defined below;

R^2 is hydrogen , C_{1-12} alkyl or aryl, optionally substituted by one or more of C_{1-4} alkyl, halogen, C_{1-4} haloalkyl, OR^4, SR^4, NO_2, CN, NR^4R^4, NR^4COR^4, $NR^4CONR^4R^4$, NR^4COR^4, $NR^4CO_2R^4$, CO_2R^4, COR^4, $CONR^4_2$, $S(O)_2R^4$, $SONH_2$, $S(O)R^4$, SO_2 NR^4R^4, $NR^4S(O)_2R^4$, wherein the C_{1-12} alkyl group optionally incorporates one or two insertions selected from the group consisting of -O-, -N(R^4)-, -S(O)- and –S(O_2)-, wherein each R^4 may be the same or different and is as defined below;

R^3 is C_{1-12} alkyl or aryl, optionally substituted by one or more of C_{1-4} alkyl, halogen, C_{1-4} haloalkyl, OR^4, SR^4, NO_2, CN, NR^4R^4, NR^4COR^4, $NR^4CONR^4R^4$, NR^4COR^4, $NR^4CO_2R^4$, CO_2R^4, COR^4, $CONR^4{}_2$, $S(O)_2R^4$, $SONH_2$, $S(O)R^4$, SO_2 NR^4R^4, $NR^4S(O)_2R^4$, wherein the C_{1-12} alkyl group optionally incorporates one or two insertions selected from the group consisting of -O-, -N(R^4)-, -S(O)- and –S(O_2)-, wherein each R^4 may be the same or different and is as defined below;

R^4 is hydrogen, C_{1-4} alkyl, or C_{1-4} haloalkyl;

R' is C_{1-12} alkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, carbocyclyl or heterocyclyl, each of which is optionally substituted, wherein:

the optionally substituted carbocyclyl or heterocyclyl group is optionally fused to one to three unsaturated, partially unsaturated or fully saturated five to seven membered rings containing zero to three heteroatoms,

each substitutable carbon atom in R', including the optional fused ring, is optionally and independently substituted by one or more of C_{1-12} alkyl, C_{3-12} cycloalkyl, C_{3-12} heterocycloalkyl, aryl, heteroaryl halogen, haloalkyl, OR^2, SR^2, NO_2, CN, NR^2R^2, NR^2COR^2, $NR^2CONR^2R^2$, NR^2COR^2, $NR^2CO_2R^2$, CO_2R^2, COR^2, $CONR^2R^2$, $S(O)_2R^2$, $SONH_2$, $S(O)R^2$, SO_2 NR^2R^2, $NR^2S(O)_2R^2$, wherein each R^2 may be the same or different and is as defined above and wherein:

the C_{1-12} alkyl group optionally incorporates one or two insertions selected from the group consisting of -O-, -C(O)-, -N(R^2)-, -S(O)- and –S(O_2)-, wherein each R^2 may be the same or different and is as defined above;

the C_{1-12} alkyl, C_{3-12} cycloalkyl, C_{3-12} heterocycloalkyl, aryl, or heteroaryl groups are optionally substituted by one or more of halogen, haloalkyl, OR^2, SR^2, NO_2, CN, NR^2R^2, NR^2COR^2, $NR^2CONR^2R^2$, NR^2COR^2, $NR^2CO_2R^2$, CO_2R^2, COR^2, $CONR^2R^2$, $S(O)_2R^2$, $SONH_2$, $S(O)R^2$,

$SO_2NR^2R^2$, $NR^2S(O)_2R^2$, wherein each R^2 may be the same or different and is as defined above; and

the C_{3-12} cycloalkyl, C_{3-12} heterocycloalkyl, aryl, or heteroaryl groups are optionally substituted by one or more C_{1-12} alkyl groups;

each saturated carbon in R', including the optional fused ring, is further optionally and independently substituted by =O, =S, NNR^2R^2, $=N\text{-}OR^2$, $=NNHCOR^2$, $=NNHCO_2R^2$, $=NNSO_2R^2$, or $=NR^2$, wherein each R^2 may be the same or different and is as defined above; and

each substitutable nitrogen atom in R' is optionally substituted by R^3, COR^2, SO_2R^2 or CO_2R^2 wherein each R^2 and R^3 may be the same or different and is as defined above;

X is NR^5; O, S or C_{1-4} alkylene that is optionally substituted by one or more of halogen, haloalkyl, OR^2, SR^2, NO_2, CN, NR^2R^2, NR^2COR^2, $NR^2CONR^2R^2$, NR^2COR^2, $NR^2CO_2R^2$, CO_2R^2, COR^2, $CONR^2R^2$, $S(O)_2R^2$, $SONH_2$, $S(O)R^2$, $SO_2NR^2R^2$, $NR^2S(O)_2R^2$, wherein each R^2 may be the same or different and is as defined above and R^5 is H, C_{1-4} alkyl, C_{1-4} alkoxy, C_{1-4} haloalkyl or C_{1-4} haloalkyl; and

Y is absent or is NR^6, O, CR^6R^6, or C_{1-4} alkylene wherein each R^6 may be the same or different and is H, C_{1-4} alkyl, C_{1-4} alkoxy or C_{1-4} haloalkyl.

3. A compound as claimed in claim 1 or claim 2, wherein R is an aryl or heteroaryl radical, optionally substituted with one or more of alkyl, haloalkyl, halogen, OR^9, SR^8, SOR^9, $N(R^9)_2$, wherein each R^9 may be the same or different and stand for hydrogen, C_{1-4} alkyl or haloalkyl.

4. A compound as claimed in any one of claims 1 to 3 wherein R is an optionally substituted aryl, preferably phenyl or napthyl.

5. A compound as claimed in claim 4, wherein R is phenyl substituted in the 3-(meta) position.

6. A compound as claimed in claim 4 or claim 5, wherein R is substituted aryl and the substituent is F, Cl or Br, preferably F; or haloalkyl, preferably CF_3, or alkyl, preferably methyl, ethyl or propyl.

7. A compound as claimed in any one of claims 1 to 6, wherein R' is C_{1-4} alkyl, alkenyl or alkynyl.

8. A compound as claimed in claim 7, wherein Y stands for an alkylene group.

9. A compound as claimed in any one of claims 1 to 6, wherein R' stands for aryl, preferably phenyl, or a heteroaryl containing up to 3 hetero atoms, or a cycloalkyl or heterocycloalkyl group, each of which may be fused to one or more aryl, heteroaryl, cycloalkyl or heterocycloalkyl rings, each optionally substituted by one or more of alkyl, halide alkyl haloalkyl, alkoxy or haloalkoxy.

10. A compound as claimed in any one of claim 1 or claims 3 to 9, wherein R'' is H, C_{1-4} alkyl (e.g. methyl, ethyl or propyl), aryl, heteroaryl, cycloalkyl or heterocycloalkyl.

11. A compound as claimed in any one of claims 1 to 10, wherein X is NR^5, most preferably NH, or a straight chain or branched C_{1-4} alkylene, e.g. methylene or ethylene;

12. A compound as claimed in any one of claims 1 to 11, wherein Y is either absent or a straight of branched chain C_{1-4}, e.g. methylene or methylmethylene.

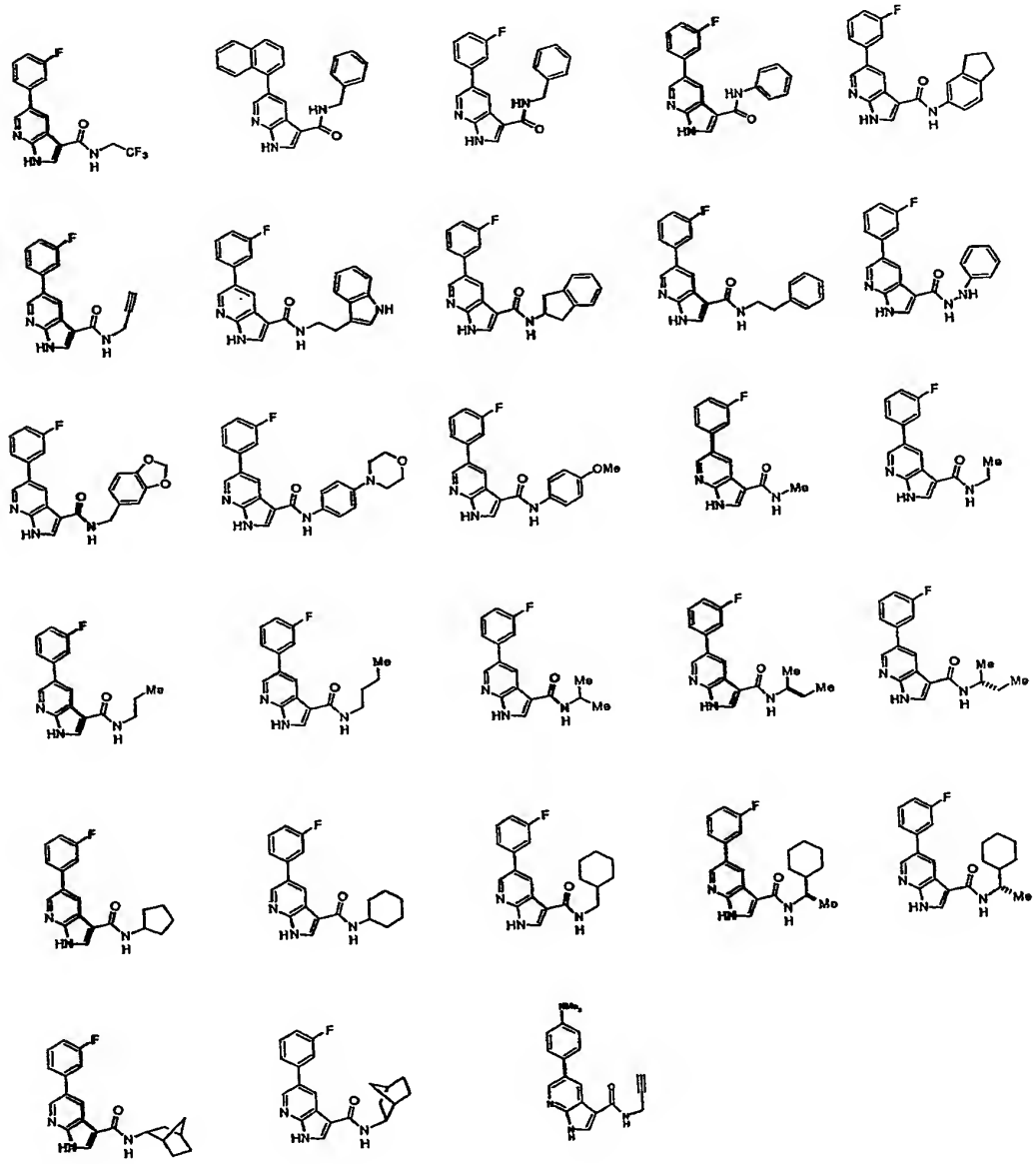
13. A compound as claimed in any one of claims 1 to 11, wherein Y is NR^6, e.g. NH, wherein R^6 is as defined in claim 1.

14. A compound as claimed in claim 13, wherein X stands for NR^5 wherein R^5 is as defined in claim 1.

15. A compound as claimed in any one of claims 1 or 3 to 14, wherein Z is

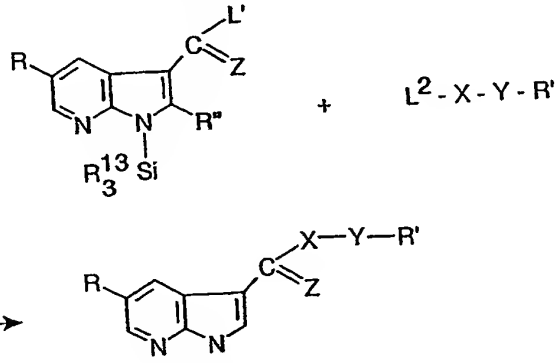
O.

16. A compound as claimed in any one of claims 1 to 15 selected from



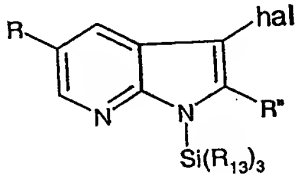
17. A prodrug of a compound as defined in any of claims 1 to 16.

18. A process for the manufacture of any one or more of the compounds of any one of claims 1 to 16 which comprises condensing a compound of the general formula (II) with the compound of the general formula (III):



in which R, R', R'' X and Y are as defined in any one of claims 1 to 16, Z is O, R^{13} stands for C_{1-6} straight or branched alkyl and L^1 and L^2 stand for radicals that together form a condensation product, e.g. H and OH, to form the compound of the general formula (I) or (Ia) as defined in any one of claims 1 to 16, in which Z stands for oxygen.

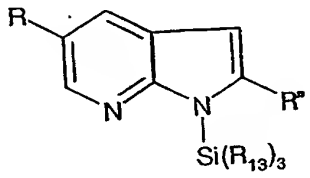
19. A process as claimed in claim 18, wherein the compound of the general formula (II) (in which Z stands for O and L^1 stands for OH) is formed by reacting a compound of the general formula (VIII)



(VIII)

in which R_{13}, R and R'' are as defined in claim 18 and hal stands for a halogen atom, preferably bromine, with an alkali metal alkyl, e.g. an alkyl lithium such as tertiary butyl lithium, and then reacting the product so obtained with CO_2.

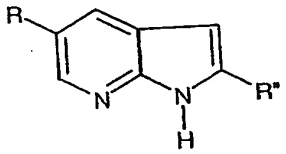
20. A process as claimed in claim 19, wherein the compound of the general formula (VIII) is formed by halogenating (preferably with bromine) the compound of the formula (VII) in the 3 position



(VII)

in which R_{13}, R and R'' are as defined in claim 18.

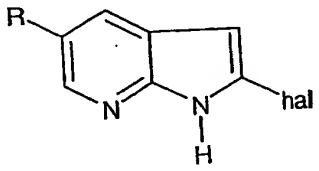
21. A process as claimed in claim 20, wherein the compound of the general formula (VII) is formed by reacting a compound of the general formula (VI)



(VI)

in which R and R'' are as defined in claim 18, with an alkali metal alkyl, e.g. an alkyl lithium such as normal or tertiary butyl lithium, followed by reacting the product so obtained with $R^{13}{}_3Si$-hal, in which R_{13}, is as defined in claim 18 and hal stands for a halogen atom.

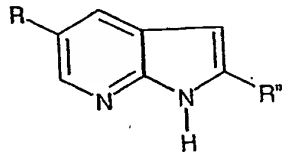
22. A process as claimed in claim 20 or 21, wherein the compound of the general formula (VI), in which R'' stands for hydrogen, is formed by hydrogenating a compound of the general formula (V):



(V)

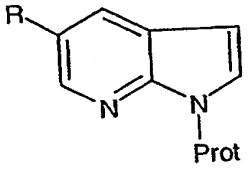
in which R is as defined in claim 18 and hal stands for a halogen atom, e.g. using hydrogen and a catalyst such as Pd-C.

23. A process as claimed in claim 21, wherein the compound of the general formula (VI), in which R'' is as defined in claim 18 except that it does not stand for hydrogen, is formed by protecting the compound of the general formula (VI),



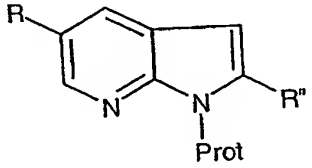
(VI)

in which R'' stands for hydrogen, in the 1 position with a suitable protecting radical, e.g. with an arylsulphonyl group, such as a phenylsulphonyl group, to form a compound of the general formula (IX)



(IX)

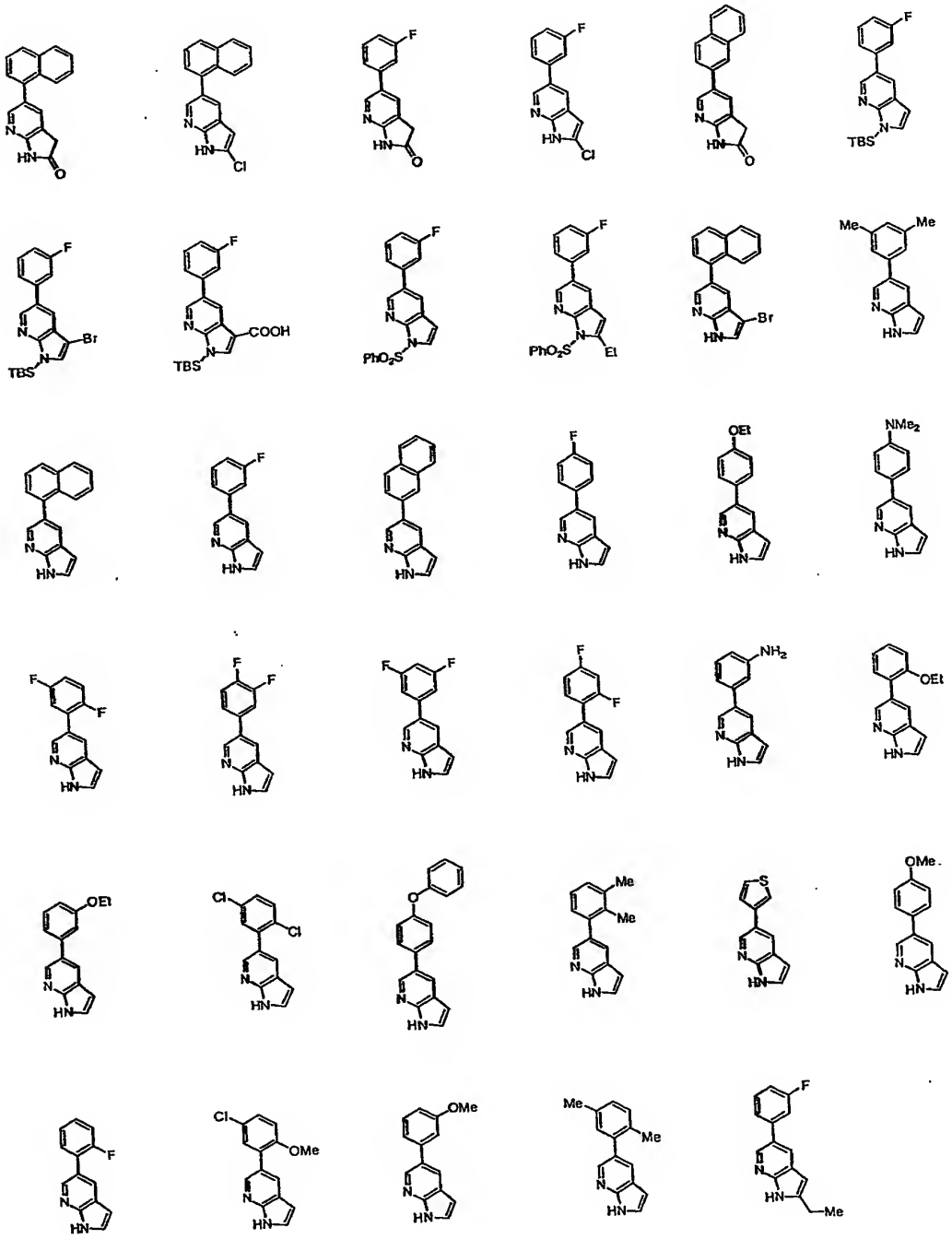
in which R is as defined in claim 18 and prot stands for the protecting group, and treating the compound of the general formula (IX) with an alkali metal alkyl, e.g. an alkyl lithium, and then with a compound R''-hal (where hal stands for a halogen, preferably iodine, and R'' is as defined in claim 18 except that it does not stand for hydrogen) to form the compound of the general formula (X)

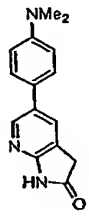


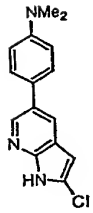
(X)

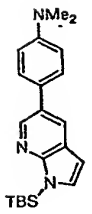
in which R and R'' are is as defined in claim 18 except that R'' does not stand for hydrogen and in which prot stands for the protecting group, and removing the protecting group, e.g. phenylsulphonyl, to form a compound of the general formula (VI) in which R and R'' are is as defined in claim 18 except that R'' does not stand for hydrogen.

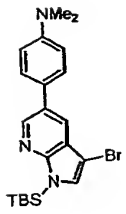
24. A process as claimed in claim 22 or 23, wherein the compound of the general formula (VI) is selected from:

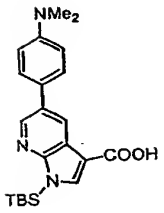




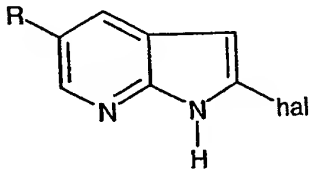








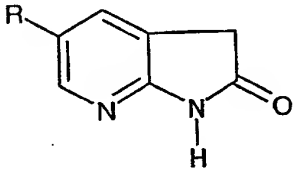
25. A process as claimed in any one of claims 22 to 24, wherein the compound of the general formula (VI), in which R'' stands for hydrogen, is formed by hydrogenating a compound of the general formula (V),



(V)

in which R is as defined in claim 18 and hal stands for a halogen atom, e.g. using hydrogen and a catalyst such as Pd-C.

26. A process as claimed in claim 25, wherein the compound of the general formula (V) is formed by halogenating a compound of the general formula (IV) in the 2 position,



(IV)

in which R is as defined in claim 18.

27. A process as claimed in any one of claims 18 to 26, which includes the further step of converting the compound of the general formula (I) in which Z stands for O into a compound of the general formula (I) in which Z stands for S or NR^7.

28. A composition comprising a compound as defined in any of claims 1-16 in combination with a pharmaceutically acceptable carrier, diluent or excipient.

29. A composition as claimed in claim 28 further comprising one or more other active agent.

30. A composition as claimed in claim 29 wherein the composition further comprises an anti-inflammatory agent, for example a p38 inhibitor.

31. A process for the manufacture of a composition as defined in any of claims 28-30, comprising combining a compound as defined in any of claims 1-16, and any additional active agent, with the pharmaceutically acceptable carrier or diluent.

32. A compound as defined in any of claims 1-16, or a composition as defined in any of claims 28-30, for use in therapy.

33. A compound as defined in any of claims 1-16, or a composition as defined in any of claims 28-30, for inhibiting JNK.

34. A compound as defined in any of claims 1-16, or a composition as defined in any of claims 28-30, for selectively inhibiting JNK3.

35. A compound as defined in any of claims 1-16, or a composition as defined in any of claims 28-30, for use in the prevention or treatment of a JNK-mediated disorder.

36. A compound or a composition as claimed in claim 35, wherein the disorder is a neurodegenerative disorder (including dementia), inflammatory disease, a disorder linked to apoptosis, particularly neuronal apoptosis, autoimmune disease, destructive bone disorder, proliferative disorder, cancer, infectious disease, allergy, ischemia reperfusion injury, heart attack, angiogenic disorder, organ hypoxia, vascular hyperplasia, cardiac hypertrophy, thrombin

induced platelet aggregation and/or any condition associated with prostaglandin endoperoxidase synthase-2.

37. A compound or composition as claimed in claim 36, wherein the neurodegenerative disorder results from apoptosis and/or inflammation.

38. A compound or composition as claimed in claim 36 or claim 37, wherein the neurodegenerative disorder is: dementia; Alzheimer's disease; Parkinson's disease; Amyotrophic Lateral Sclerosis; Huntington's disease; senile chorea; Sydenham's chorea; hypoglycemia; head and spinal cord trauma including traumatic head injury; acute and chronic pain; epilepsy and seizures; olivopontocerebellar dementia; neuronal cell death; hypoxia-related neurodegeneration; acute hypoxia; glutamate toxicity including glutamate neurotoxicity; cerebral ischemia; dementia linked to meningitis and/or neurosis; cerebrovascular dementia; or dementia in an HIV-infected patient.

39. A compound or composition as claimed in claim 36 or 37, wherein the neurodegenerative disorder is a peripheral neuropathy, including mononeuropathy, multiple mononeuropathy or polyneuropathy, such as may be found in diabetes mellitus, Lyme disease or uremia; peripheral neuropathy caused by a toxic agent; demyelinating disease such as acute or chronic inflammatory polyneuropathy, leukodystrophies or Guillain-Barré syndrome; multiple mononeuropathy secondary to a collagen vascular disorder (e.g. polyarteritis nodosa, SLE, Sjögren's syndrome); multiple mononeuropathy secondary to sarcoidosis; multiple mononeuropathy secondary to a metabolic disease (e.g. diabetes or amyloidosis); or multiple mononeuropathy secondary to an infectious disease (e.g. Lyme disease or HIV infection).

40. A compound or composition as claimed in claim 36, wherein the disorder is inflammatory bowel disorder; bronchitis; asthma; acute pancreatitis; chronic pancreatitis; allergies of various types; Alzheimer's disease; autoimmune disease such as rheumatoid arthritis, systemic lupus erythematosus, glumerulonephritis, scleroderma, chronic thyroiditis, Graves's disease, autoimmune gastritis, diabetes,

autoimmune haemolytis anaemia, autoimmune neutropaenia, thrombocytopenia, atopic dermatitis, chronic active hepatitis, myasthenia gravis, multiple sclerosis, ulcerative colitis, Crohn's disease, psoriasis or graft vs host disease.

41. A method of treating or preventing a JNK-mediated disorder in an individual, which method comprises administering to said individual a compound as claimed in any of claims 1-16 or a composition as claimed in any of claims 28-30.

42. A method as claimed in claim 41, wherein the individual is in need of the treatment or prevention of the disorder.

43. A method as claimed in claim 41 or 42, wherein the disorder is a neurodegenerative disorder (including dementia), inflammatory disease, a disorder linked to apoptosis, particularly neuronal apoptosis, autoimmune disease, destructive bone disorder, proliferative disorder, cancer, infectious disease, allergy, ischemia reperfusion injury, heart attack, angiogenic disorder, organ hypoxia, vascular hyperplasia, cardiac hypertrophy, thrombin induced platelet aggregation and/or any condition associated with prostaglandin endoperoxidase synthase-2.

44. A method as claimed in claim 43, wherein the neurodegenerative disorder results from apoptosis and/or inflammation.

45. A method as claimed in claim 43 or 44, wherein the neurodegenerative disorder is: dementia; Alzheimer's disease; Parkinson's disease; Amyotrophic Lateral Sclerosis; Huntington's disease; senile chorea; Sydenham's chorea; hypoglycemia; head and spinal cord trauma including traumatic head injury; acute and chronic pain; epilepsy and seizures; olivopontocerebellar dementia; neuronal cell death; hypoxia-related neurodegeneration; acute hypoxia; glutamate toxicity including glutamate neurotoxicity; cerebral ischemia; dementia linked to meningitis and/or neurosis; cerebrovascular dementia; or dementia in an HIV-infected patient.

46. A method as claimed in claim 43 or 44, wherein the neurodegenerative disorder is a peripheral neuropathy, including mononeuropathy, multiple mononeuropathy or polyneuropathy, such as may be found in diabetes mellitus, Lyme disease or uremia; peripheral neuropathy caused by a toxic agent; demyelinating disease such as acute or chronic inflammatory polyneuropathy, leukodystrophies or Guillain-Barré syndrome; multiple mononeuropathy secondary to a collagen vascular disorder (e.g. polyarteritis nodosa, SLE, Sjögren's syndrome); multiple mononeuropathy secondary to sarcoidosis; multiple mononeuropathy secondary to a metabolic disease (e.g. diabetes or amyloidosis); or multiple mononeuropathy secondary to an infectious disease (e.g. Lyme disease or HIV infection).

47. A method as claimed in claim 41, 42 or 43, wherein the disorder is inflammatory bowel disorder; bronchitis; asthma; acute pancreatitis; chronic pancreatitis; allergies of various types; Alzheimer's disease; autoimmune disease such as rheumatoid arthritis, systemic lupus erythematosus, glumerulonephritis, scleroderma, chronic thyroiditis, Graves's disease, autoimmune gastritis, diabetes, autoimmune haemolytis anaemia, autoimmune neutropaenia, thrombocytopenia, atopic dermatitis, chronic active hepatitis, myasthenia gravis, multiple sclerosis, ulcerative colitis, Crohn's disease, psoriasis or graft vs host disease.

48. A method as claimed in any of claims 41-47, wherein one or more other active agent is administered to the individual simultaneously, subsequently or sequentially to administering the compound.

49. A method as claimed in claim 48, wherein the other active agent is an anti-inflammatory agent such as a p38 inhibitor.

50. Use of a compound as defined in claim 1-16 in the manufacture of a medicament for the prevention or treatment of a JNK-mediated disorder.

51. Use as claimed in claim 50, wherein the disorder is a neurodegenerative disorder (including dementia), inflammatory disease, a disorder linked to apoptosis, particularly neuronal apoptosis, autoimmune disease, destructive bone disorder, proliferative disorder, cancer, infectious disease, allergy, ischemia reperfusion injury, heart attack, angiogenic disorder, organ hypoxia, vascular hyperplasia, cardiac hypertrophy, thrombin induced platelet aggregation and/or any condition associated with prostaglandin endoperoxidase synthase-2.

52. Use as claimed in claim 51, wherein the neurodegenerative disorder results from apoptosis and/or inflammation.

53. Use as claimed in claim 51 or 52, wherein the neurodegenerative disorder is: dementia; Alzheimer's disease; Parkinson's disease; Amyotrophic Lateral Sclerosis; Huntington's disease; senile chorea; Sydenham's chorea; hypoglycemia; head and spinal cord trauma including traumatic head injury; acute and chronic pain; epilepsy and seizures; olivopontocerebellar dementia; neuronal cell death; hypoxia-related neurodegeneration; acute hypoxia; glutamate toxicity including glutamate neurotoxicity; cerebral ischemia; dementia linked to meningitis and/or neurosis; cerebrovascular dementia; or dementia in an HIV-infected patient.

54. Use as claimed in claim 51 or 52, wherein the neurodegenerative disorder is a peripheral neuropathy, including mononeuropathy, multiple mononeuropathy or polyneuropathy, such as may be found in diabetes mellitus, Lyme disease or uremia; peripheral neuropathy caused by a toxic agent; demyelinating disease such as acute or chronic inflammatory polyneuropathy, leukodystrophies or Guillain-Barré syndrome; multiple mononeuropathy secondary to a collagen vascular disorder (e.g. polyarteritis nodosa, SLE, Sjögren's syndrome); multiple mononeuropathy secondary to sarcoidosis; multiple mononeuropathy secondary to a metabolic disease (e.g. diabetes or amyloidosis); or multiple mononeuropathy secondary to an infectious disease (e.g. Lyme disease or HIV infection).

55. Use as claimed in claim 51, wherein the disorder is inflammatory bowel disorder; bronchitis; asthma; acute pancreatitis; chronic pancreatitis; allergies of various types; Alzheimer's disease; autoimmune disease such as rheumatoid arthritis, systemic lupus erythematosus, glumerulonephritis, scleroderma, chronic thyroiditis, Graves's disease, autoimmune gastritis, diabetes, autoimmune haemolytis anaemia, autoimmune neutropaenia, thrombocytopenia, atopic dermatitis, chronic active hepatitis, myasthenia gravis, multiple sclerosis, ulcerative colitis, Crohn's disease, psoriasis or graft vs host disease.

56. Use as claimed in any of claims 50-55, wherein the medicament further includes one or more other active agent.

57. Use as claimed in claim 56, wherein the other active agent is an anti-inflammatory agent such as a p38 inhibitor.

58. An assay for determining the activity of the compounds as defined in any of claims 1-16, comprising providing a system for assaying the activity and assaying the activity of a compound as defined in any of claims 1-16.

59. An assay as claimed in claim 58, wherein the assay is for the JNK inhibiting activity of the compound, preferably for the JNK3-specific inhibiting activity of the compound.

60. An assay as claimed in claim 58 or 59, wherein the assay is a Scintillation Proximity Assay (SPA) using radiolabelled ATP, or is ELISA.

61. A method of inhibiting the activity or function of a JNK, particularly JNK3, which method comprises exposing a JNK to a compound as defined in any of claims 1-16 or a composition as defined in any of claims 28-40.

62. A method as claimed in claim 61, which is performed in a research model.

63. A method as claimed in claim 62, wherein the research model is an animal model.